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ORGANOTHERAPY IN GENERAL PRACTICE NO. 3  
ASTHENIA HYPOTHYROIDISM HYPOADRENIA SENILITY

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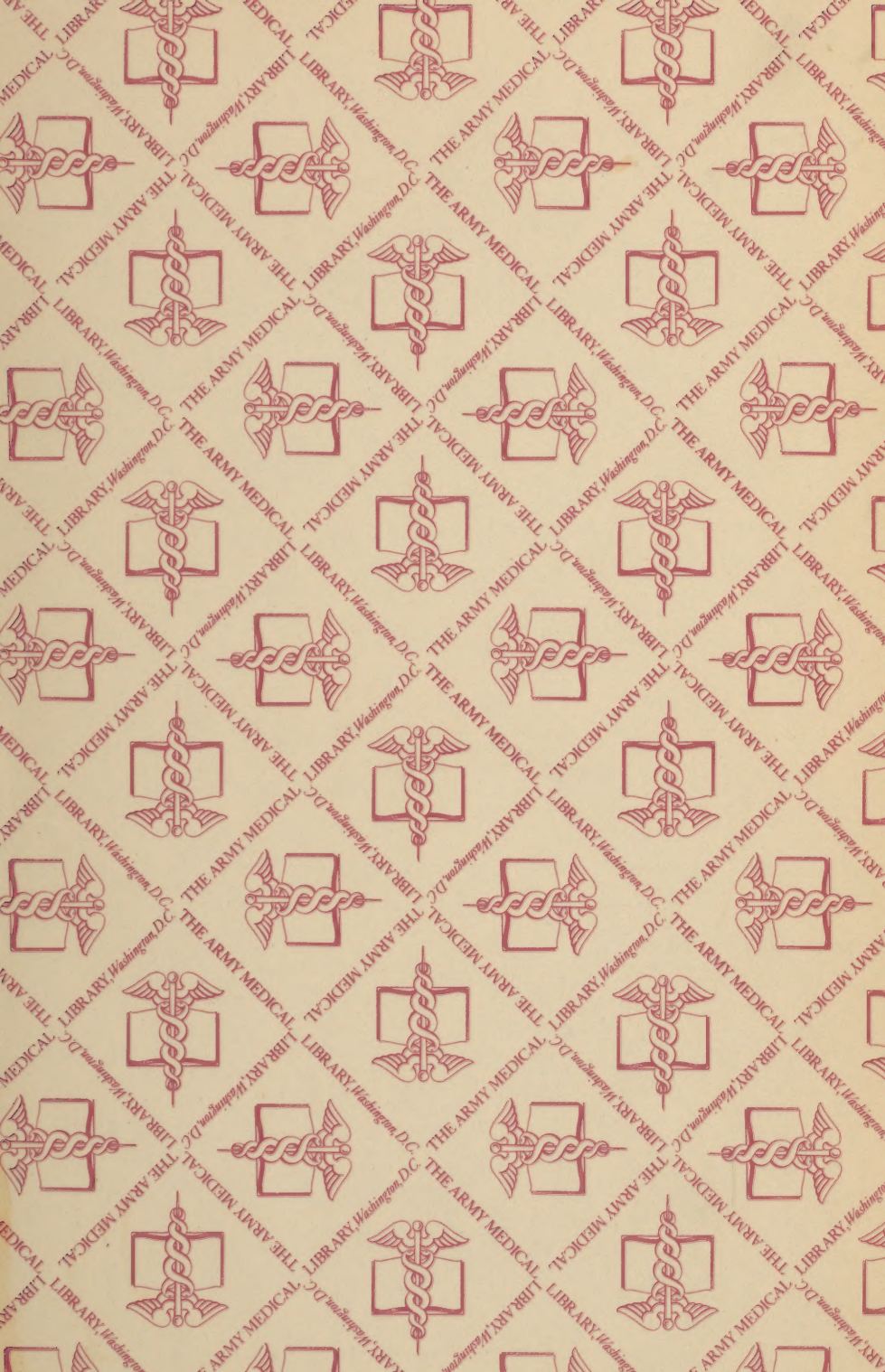
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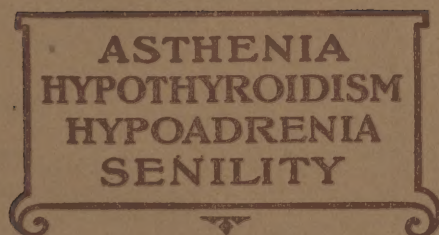




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# ORGANOTHERAPY *in* GENERAL PRACTICE

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# ASTHENIA, HYPOTHYROIDISM, HYPOADRENIA, SENILITY

The treatment of general debility and of states of lowered vitality in which no demonstrable pathologic process is present has always been a stumbling block for the general practitioner. Organotherapy now offers a solution to this problem in that it introduces substances which directly stimulate cell metabolism and raise metabolic rate. The successful treatment of these conditions has, therefore, become possible. Of course, the pathology in these conditions is comparatively unknown — that is, there is no structural defect, but a functional derangement due to glandular deficiency. Following extended illness, states of exhaustion and the infections, and occurring as a result of the burdens and conditions imposed by various walks of life, these conditions have been treated by “tonics,” “alteratives,” etc. Only too frequently the “tonic” has been some substance designed to increase appetite and digestive capacity, in the belief that lack of strength results from some primary lack of nutrition. The following discussion, it is hoped, will indicate a better therapy.

## ASTHENIA

Asthenia is a symptom characteristic of almost all disease, both infectious and metabolic, and may also, and frequently does, manifest itself as the principal or only symptom in conditions in which there is no demonstrable pathology. It constitutes one of the commonest conditions that the general practitioner is called upon to treat and includes patients recovering from definite illness, prolonged infections and states of general lowered vitality. For these reasons a rather extensive investigation of the causes of asthenia and the general nature of the conditions under which it appears is of more than ordinary interest to the physician. Asthenia, as here used, is but slightly, if any, more inclusive than the term “myasthenia.” It is mere weakness, the “run-down feeling,” for which some effective treatment is necessary. The train of associated symptoms, undue fatigability, cardiac insufficiency, feeble pulse, arterial hypotension, arrhythmia, bradycardia, vasomotor disturbances, cold extremities, etc., which together make up a complete clinical picture



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of debility, will be considered in the following discussion of hypoadrenia. Asthenia may occur, however, as a result of disturbances of both the pituitary and thyroid, as well as of the adrenals. In the frequently encountered clinical conditions characterized by lowered basal metabolism and lessened functional activity of the acceleratory group of endocrine organs, asthenia is conspicuous. The energy production of the organism and the cell metabolism are at fault and the subjective symptom, asthenia, arises.

Sejary<sup>1</sup> distinguishes between asthenia due to suprarenal insufficiency and those due to other causes. The adrenal type is characterized by rapid muscle exhaustion and fatigability, whereas other types show a diminution of muscular force but not a rapid exhaustion. According to Sejary, it is as yet unproved that any other asthenia of endocrine origin can present this special type of rapid exhaustion of muscular force. Asthenia forming a part of the Erb-Goldflamm syndrome may be mentioned as a variety occurring independently of the endocrine system, although even this has been suggested as of adrenal origin. Harvier says<sup>2</sup>:

"Certain cases of myasthenia which are included in the syndrome of Erb-Goldflamm, characterized by muscular asthenia (weakness of the muscles, tendency to be easily tired), either diffuse or limited to certain muscles of the face, are probably due to some adrenal disturbance. They improve under adrenal medication, alone or combined with thyroid or pituitary extract."

Sejary, however, differentiates it from the adrenal type by the paralysis of the oculomotor and facial muscles, and those of the neck, conditions not present in the adrenal type, which shows no especial predilection for the muscles innervated by the cerebral nerves.

**Pathology of Fatigue** A study of the fatigue process gives some aid in understanding the nature of asthenia, which is the conscious sense of muscle inefficiency. Many experimental studies of fatigue have been made and at least something is known of the conditions in which it arises. It seems fairly well established that an accumulation of the waste products of catabolism, "fatigue substances," are directly concerned in the condition. In some cases a second possibility is present — that of a too rapid consumption of the material necessary for the work of muscle contraction — but this need not be considered here. Ranke made the first comprehensive investigations of fatigue pathology and suggested the name "fatigue substances" for those compounds which, when present in sufficient concentration, inhibit muscle contractions. He showed that extracts of fatigued muscle, when injected into the circulation of a fresh animal artificially produced fatigue, whereas extracts of fresh muscle substance (not fatigued) gave no such results. That such substances are actually formed and are largely responsible for muscle fatigue seems fairly certain from the nature of the various experimental results and from clinical

<sup>1</sup>A. Sejary, *La Presse Médicale*, Jan. 28, 1922.

<sup>2</sup>*Endocrine Glands and the Sympathetic System*, 1922.



experience. Such substances produced in one set of muscles affect not only that particular set but, diffused through the circulation, definitely lower the efficiency of other muscle groups and cause the general malaise and psychic dullness incident to fatigue of the organism as a whole. Lactic acid appears to be chief among these fatigue substances and in muscle preparations fatigue may be produced by bathing or perfusion with lactic acid solutions. Aqueous solutions of muscle previously exhausted to the point of fatigue also reduce the excitability of the muscle preparation and induce the fatigue condition. In experiments in which the muscle is not cut off from its circulation and in which the accumulation of these substances is more difficult, fatigue is much less readily produced than in those isolated preparations in which the conditions for accumulation are ideal. In either class of preparations the fatigue may be relieved by flushing with normal salt solution.

The action of these fatigue substances may be either in the muscle itself or in the myoneural junction—the receptive substance—of the nerve ending: less likely does it appear that they act through the nerve tracts themselves.

What conditions permit the accumulation of the toxic wastes responsible for asthenia and the fatigue syndrome? Chief among these is lack of oxygen and the resulting state of suboxidation and lowered metabolism.

“It seems more probable that we are dealing here with two stages of one process and that in the muscle under normal conditions (that is, richly supplied with oxygen) the first chemical change is one of disintegration, leading to the formation of lactic acid (and probably other substances), and that this is followed by a process of oxidation, in which all the products of the first stage are converted into  $\text{CO}_2$ , which can be rapidly eliminated from the muscle. If the supply of oxygen is deficient, the products of the first stage remain in the muscle, giving rise to the phenomena of fatigue.<sup>1</sup>”

The effect of oxygen gas in relieving fatigue and restoring the irritability of muscle preparations previously exhausted is evidence of the influence of oxygen in preventing the onset of the fatigue syndrome. With a free supply of oxygen, the excessive accumulation of lactic acid, with its inhibitions to muscle contractions, does not take place. Lactic acid is formed as a result of the work performed by the muscles and may be an intermediary product of sugar metabolism. A certain acid concentration appears to be necessary for contraction, however, and it is probable that even in ideal conditions of oxidation the lactic acid is not finally and wholly oxidized but rather is synthesized into the substances from which it was formed. Suboxidation, therefore, causes fatigue through permitting *excessive* accumulation of the acid.

“In the process of recovery which follows the activity of muscle when it is allowed to rest, it is found that the lactic acid disappears provided a supply of oxygen is available. Since at the same time carbon dioxide is set free from the muscle,

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<sup>1</sup> *Human Physiology*, Starling, 1912.

one might suspect that the disappearance of the lactic acid is due to its being oxidized to carbon dioxide and water. This, however, cannot be the case, for it is known that after the repeated fatigue and recovery of an isolated muscle the total quantity of lactic acid which may be extracted from it is undiminished. In other words lactic acid does not disappear from the muscle during rest, but is restored to the condition in which it occurred before contraction took place. Further evidence that lactic acid is not oxidized is afforded by the fact that the disappearance of 1 gram of lactic acid from fatigued muscle is accompanied by the production of 450 calories of heat, whereas the oxidation of 1 gram of lactic acid would set free 3700 calories. Apparently the oxidation of some other substance is necessary in order to restore lactic acid to the precursor condition, and to replace the potential energy lost in the contractile process, and in the course of the oxidation of this substance — carbon dioxide is liberated and heat is given off. The nature of the substance oxidized is not definitely known, but it is presumed from the high respiratory quotient of muscular work that it is chiefly carbohydrate."<sup>1</sup>

### **Adrenal Influence**

Asthenia is undoubtedly the most conspicuous and characteristic symptom of adrenal insufficiency, and the function of epinephrin in the maintenance of voluntary muscle efficiency is very striking. Cannon, Gruber, Fellows and others have shown that epinephrin increases the contractility of the voluntary muscles and diminishes the tendency to muscle fatigue. Gruber reached the following conclusions<sup>2</sup>:

"In the fatigued unaltered nerve muscle adrenalin may increase the height of muscular contraction by a twofold action, by improvement of the blood supply (vasodilation) and by its chemical action upon some substances in the muscle.

"In a muscle in which the nerve is cut and stimulated, adrenalin in small doses, however administered, does not better the circulation and must therefore produce its effect of increasing the height of muscular contraction by its chemical (specific) action alone.

"The following three processes which normally go on in the muscle may be greatly accelerated by adrenalin and it is not improbable that one or all of these will finally prove to be the way in which adrenalin produces its effects:

"1. The conversion of glycogen into sugar.

"2. The reconversion of lactic acid into sugar (transformation of fatigue products).

"3. The oxidizing of lactic acid into carbon dioxide and water (destruction of fatigue products)."

Gruber and Kretschmer<sup>3</sup> in experiments upon cats found that:

<sup>1</sup>"Physiology and Biochemistry in Modern Medicine," MacLeod, 1922.

<sup>2</sup>*American Journal of Physiology*, 1917, Vol. 43.

<sup>3</sup>*American Journal of Physiology*, 1918, Vol. 47.



"Adrenalin (0.5 to 1 c. c. of 1:1,000 solution) counteracts the induced fatigue produced by the perfusion of fatigue substances such as sarcolactic acid, lactic acid and acid potassium phosphate, through the muscle in identically the same way as it does the fatigue produced normally in active muscles."

Hartmann<sup>1</sup> investigated the effect of epinephrin upon muscular activity and has shown a very definite relationship between epinephrin output and muscular response. He finds that in normal animals there is an increase in epinephrin output during exercise, which output is greater in proportion to the length and vigor of the exercise. This increased epinephrin output persists after the exercise ceases, the duration depending to some extent upon the amount of work performed. Hartmann also found that intramuscular injection of adrenalin improved the output of work in many normal cats and in cats with epinephrin deficiency, and that an animal can go further and travel faster when there is an increase in the epinephrin output during exercise. Hartmann makes an interesting explanation of the so-called "second wind" of athletes, which he relates to the increased efficiency resulting from epinephrin. He believes that epinephrin is an important factor in the development of "second wind" or that state of increased efficiency which takes place after a condition of exhaustion has apparently developed.

In investigations made by Hartmann, Waite and Powell<sup>2</sup> they came to the conclusion:

"Our results seem to indicate that epinephrin plays a very important role in increasing muscular work and delaying the onset of fatigue."

The influence of epinephrin seems to be due to a direct specific influence upon the muscle cell and this conclusion has been reached by various investigators. Gruber<sup>3</sup> finds that, while in some of the experiments the increased height of the muscular contraction may be accounted for by increased circulation through the muscle, there are specific effects in eliminating fatigue. The manner in which the specific action is accomplished is unknown and may be due to the neutralization or destruction of the fatigue products, the rapid formation of more available energy, or to some toxic action increasing the excitability of the muscle.

It has been suggested by MacLeod (see above) that the oxidation of some substance, presumably carbohydrate, is necessary to prevent the excessive accumulation of lactic acid and to restore it to the precursor substance, a mode of action also suggested by Hartmann (transformation of fatigue products). There has been much evidence to show that the adrenals are important factors in sugar metabolism (Bierry, Malloizel, Cannon, Porges) and, although such influence is minimized by some, the evidence is very suggestive of an action in sugar metabolism which, in part at least, accounts for the epinephrin effect in relieving fatigue.

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<sup>1</sup>Endocrinology, July, 1922.

<sup>2</sup>American Journal of Physiology, 1922, Vol. 60, No. 2.

<sup>3</sup>Endocrinology, 1919, Vol. 3, No. 2.



"The asthenia which dominates the clinical picture of adrenal insufficiency may be explained by the undoubted fact that adrenalin presides over carbohydrate metabolism. As for the latter view, it is true that adrenalin regulates the deposit of glycogen in the liver and its transformation into glucose; if adrenalin is deficient, carbohydrate metabolism is interfered with and muscular action is rendered impossible."

It should be mentioned, too, that the effects of the cortex, which are important in producing other symptoms of hypoadrenia, may also be a factor in producing the asthenia. The evidence, however, points strongly to the epinephrin as the essential factor.

In marked muscle fatigue the quantity of epinephrin in the adrenals themselves is much reduced and in the light of Hartmann's observations above this appears to indicate that in the maintenance of muscle efficiency, following the demands of excessive contraction, all the available epinephrin is consumed, and fatigue develops when the store has been exhausted and epinephrin is no longer available. Vacuole formation in the cortical portion is also noted and indicates some function of this portion of the gland in muscle work.

## HYPOADRENIA

Hypoadrenia or suprarenal insufficiency has been described under various names and divided into various classifications, for the most part depending upon the duration, and the extent and character of the symptoms. In 1899 Sargent, in association with Leon Bernard, made what appears to have been the first description of a case of suprarenal insufficiency not Addisonian in character. Addison's disease is an extreme example, representing the upper limit of suprarenal insufficiency, and the milder cases of clinical hypoadrenia, the existence of which has been challenged by some workers in experimental physiology and pathology, represent the lower limit.

The symptoms of actual extirpation of the adrenals include rapidly developing asthenia (myasthenia), convulsions, psychic depression, cardiac weakness, lowered temperature and blood pressure, dyspnea, etc. In some of the acute forms of suprarenal insufficiency (suprarenal hemorrhage) symptoms approximating these may be observed. The onset is sudden and the course rapid and fatal. Acute gastrointestinal symptoms — vomiting, diarrhea, etc. — may be marked. In Addison's disease the asthenia is an outstanding symptom and there is also another perhaps equally characteristic, the discoloration or bronzing of the skin, that is not apparent in other forms of insufficiency. The asthenia has been described above. Epinephrin appears to play an important part in muscle work and fatigue, and there is much evidence that the myasthenia at least is due to deficiency of this substance. It should be made plain that the evidence in favor of epinephrin deficiency as a

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<sup>1</sup>G. Fiore, *Pensiero Medico*, Jan. 1, 1922.

cause of the symptom asthenia is much stronger and generally less open to question than as a cause of low blood pressure and other symptoms of hypoadrenia, in which physiological research at least seems to have shown that epinephrin does not play such an important part. The blood pressure is characteristically low. It is not possible to state just what defect of the suprarenal glands is responsible for this condition, but it forms a fairly constant feature of hypoadrenia and there can be no doubt but that the suprarenal medulla or cortex, or both, are essential in the maintenance of vascular tone and circulatory efficiency. Feeble heart action is a concomitant of the low pressure and is explicable in the light of the known stimulatory action of epinephrin on cardiac muscle and the lack of tonicity resulting in all contractile cells as a result of the accumulation of the products of lowered metabolism. Josué<sup>1</sup> described a special type of cardiac affection—cardiac asystole—in which suprarenal insufficiency appeared to be the cause. There were cases with demonstrable hypertrophy and both systolic and diastolic pressures were constantly low, and three of the four cases showed marked arrhythmia and auricular fibrillation and the symptoms of dyspnea, pulmonary and hepatic congestion and edema. Although histologic examination showed a comparatively normal condition of the cardiac muscle fibres, the suprarenals were in all the cases very small, degenerated and giving every evidence of much decreased functional activity in life. Metabolism in general is reduced, an effect that may be due to either the impaired function of the cortex or medulla. An appreciable reduction in the blood sugar takes place.

### Gastro-Intestinal Symptoms

The gastric, intestinal and digestive symptoms observed in extirpation experiments are evident in lesser degree in the milder clinical forms, and vomiting, diarrhea, anorexia, dyspepsia, etc., are common. Loeper<sup>2</sup> has described a type of indigestion caused by suprarenal insufficiency, characterized by gastric distress and constipation, the pain arising in from half an hour to two hours after eating. This is attended by asthenia, low blood pressure and general depression, all of which improve with the improvement in the suprarenal factor. An interesting and not satisfactorily explained association of gastric and gastro-duodenal ulcers with disease of the adrenals may be noted. Silvestri<sup>3</sup> concludes that these are chiefly the result of the predominance of the vagus system and that when there is a good balance of the endocrine system these ulcers are not formed. The vagus influence may be accentuated by stimuli from the sex glands, for castration at pregnancy depresses the vagus activity and cures the ulcers, while partial or total removal of the suprarenals causes gastric and duodenal ulcers. It would seem that the experimental suprarenal insufficiency produced by Silvestri may produce ulcers by removing the antagonistic effects of the sympathetic system ordinarily stimulated by the suprarenals.

<sup>1</sup>O. Josué and F. Belloir, *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris*, April 9, 1914.

<sup>2</sup>Loeper, "Leçons de Pathologie Digestive."

<sup>3</sup>Silvestri, *Il Policlinico*, June 28, 1920.

In experimental insufficiency, effects upon the body temperature are evident. Scott<sup>1</sup> found that in suprarenal insufficiency amounting practically to suppression, there is a decrease of heat production and death. In less severe injury and consequent lesser insufficiency (in cats) there is a "profound effect upon the calorific mechanism, characterized by a significant increase in heat production." Probably in the clinical types marked variations in temperature are complicated with abnormal function of other endocrine glands.

## TYPES OF HYPOADRENIA

Sajous classifies hypoadrenia as:

1. Functional hypoadrenia,
2. Progressive hypoadrenia,
3. Terminal hypoadrenia,

a classification which, for the practical purposes of clinical medicine is as good as any proposed, although numerous others have appeared.

### Effects of Infection, Toxemia and Defective Diet

The adrenals show marked changes following acute infections, and nutritional disturbances and chronic infections as well are accompanied by changes in the glands. McCarrison found that the functional activity of the adrenal glands is dependent on the quality of the food,<sup>2</sup> and that in animal experiments the adrenal glands enlarge in consequence of qualitatively deficient food. He finds as a result of his studies that: "An intimate relationship exists between the adrenal glands and the metabolic processes of the animal organism." Particularly following influenza is the involvement of the adrenals very common and the pronounced prostration characteristic of this condition seems to depend upon this adrenal factor. Hypoadrenia is also characteristically found following typhoid fever, pneumonia, diphtheria, scarlet fever, malaria, tuberculosis, etc. This is the "terminal" hypoadrenia of Sajous, described by him as due to exhaustion of the glands during the acute febrile period of the infection. The adrenals appear to be peculiarly susceptible to infection or toxins of any kind, and continued irritation of toxic substances may result in a condition of permanently lowered functional activity.

The relation of the adrenals to the emotions, the "emergency" theory of Cannon, seems to bear application to certain types of insufficiency arising as a result of psychic causes — intense emotion, etc. A class of cases common during and after the war is of this kind. Asthenia, low blood pressure, pronounced psychic symptoms, circulatory disturbances and inability to assemble the bodily resources for rapid, unusual demands, appear to be due to adrenal insufficiency resulting from previous heavy and overwhelming demands upon the adrenal apparatus. Satre has described such conditions in soldiers and believes the mental and physical overexertion of the soldier leads to exhaustion of the endocrine and other organs. Shock he believes is *per se* largely a condition of adrenal insufficiency.

<sup>1</sup>W. J. N. Scott, *Journal of Experimental Medicine*, Aug. 1, 1922.

<sup>2</sup>McCarrison, "Studies in Deficiency Disease," 1921.



## FUNCTIONAL HYPOADRENIA

### Definition of Functional Hypoadrenia

"Functional hypoadrenia is the symptom complex of deficient activity of the adrenals, due to inadequate development, exhaustion by fatigue, senile degeneration, or any other factor which, without provoking organic lesions in the organs or their nerve paths, is capable of reducing their secretory activity. Asthenia, sensitiveness to cold and cold extremities, hypotension, weak cardiac action and pulse, anorexia, anemia, slow metabolism, constipation, and psychasthenia are the main symptoms of this condition.<sup>1</sup>

This form of hypoadrenia is encountered at four periods of life: infancy, childhood, adult and old age, and includes the asthenias of these periods usually described as resulting from "weakness or exhaustion." (Sajous.) This type may be due to a congenital underdevelopment of the adrenal tissue, a conception which has found frequent expression in the literature and which might account for an adrenal insufficiency type.

"There is a very large, not very well defined, but very important field, which is characterized by so slight a degree of suprarenal insufficiency that it is called *myopragia congenita* of the suprarenals. It is constitutional, hereditary or acquired through infection or toxins. This myopragia, whether constitutional, congenital, hereditary or acquired, may have for its pathological basis a hypoplasia or simply a functional insufficiency of the suprarenals, which has been caused by some dystrophy resulting from a disease in the ascendants, especially tuberculosis and syphilis. According to Wiesel, this condition is caused by the status thymico-lymphaticus and with it is often associated the syndrome of constitutional vagotonia, eosinophilia, exudative diathesis, and we are led to believe that the basis of these conditions is a constitutional suprarenal insufficiency." (Pende.)

Functional hypoadrenia may be self limited and undergo spontaneous recovery. The removal of the excessive demands upon the function is usually followed by some improvement in the symptoms. The mental attitude is frequently characteristic and one of indecision, lack of initiative and tendency to melancholia.

Experimental physiology has not contributed any brilliant results in establishing a condition of artificial hypoadrenia, a fact which has led to some physiologists adopting a somewhat skeptical attitude toward the clinical varieties of adrenal insufficiency. The criticism arising from this class of workers has shown such a disregard for the facts of clinical medicine, and the limitations of the experimental method are so apparent, that it fails to carry conviction or bear the importance which properly interpreted physiological investigation should. In a reply to criticism of this kind, Sergeant<sup>2</sup> gives a comprehensive review of the clinical views

<sup>1</sup>Sajous, "The Internal Secretions and the Principles of Medicine," 10th Edition, 1922.

<sup>2</sup>E. Sergeant, *La Presse Médicale*, Oct. 12, 1921.

of the condition, following the first described case (his own) in 1893. Sargent disposes of the criticism that clinicians generally attribute the symptoms of suprarenal insufficiency (including Addison's disease) to insufficient epinephrin production by showing that at the time of the first description of this condition epinephrin was unknown and that clinical views since (including his own) have generally regarded the condition as an insufficiency of the whole gland. Pende clearly recognizes the influence of the whole suprarenal in giving rise to the symptoms of insufficiency:

"The cortex and medulla are so intimately connected that it is not possible to imagine functional efficiency of one without that of the other. This intimate connection may be traced all the way up in the scale of the vertebrates, being more and more intimate and complicated as we pass from the lower to the higher. In the lower animals, their functions are perfectly distinct, but as we approach the mammalia they become more and more inseparable. It seems as if we were justified in inferring that the syndrome of medullary insufficiency is not alone caused by the lack of adrenalin in the blood. Rather are we inclined to think that many of the symptoms of adrenalin deficiency, which we find in animals that have been deprived of their suprarenals, are due to unknown but strictly necessary connections between the medulla and the cortex."

Sajous<sup>1</sup> also emphasizes the error of assuming that clinicians attribute Addison's disease to an epinephrin insufficiency. There seems little doubt but that the syndrome of suprarenal insufficiency — asthenia, hypotension, feeble and irregular heart action, vasomotor instability, gastric and other digestive disturbances, lowered metabolism, psychic depression, etc. — is due to insufficiency of both parts, cortex and medulla, as it has been shown in convincing manner that death in extirpation experiments is due to loss of the cortex, while total suppression of the epinephrin output is followed by impaired metabolism, for, although numerous observers have shown that the concentration of epinephrin in the circulating blood is normally very small, even physiologists who have most critically examined the facts of the role of epinephrin in the organism do not deny a physiological function. "Small as the concentration of epinephrin may be in arterial blood, there is evidence that it may exert a certain action."<sup>2</sup>

That suprarenal insufficiency is due to an insufficiency of the whole gland is suggested by injection experiments using suprarenal extract, resulting in effects not obtainable with epinephrin. In the treatment of Addison's disease, an extreme case of insufficiency, the treatment is with whole gland and not by epinephrin. "Either the fresh gland or a glandular extract or the dried gland, all representing the whole gland, must be used to expect beneficial results, as shown by a personal study of 120 reported cases."<sup>3</sup>

<sup>1</sup>C. E. deM. Sajous, *Endocrinology*, March, 1922.

<sup>2</sup>Stewart, "Endocrinology and Metabolism," Vol. II, 1922.

<sup>3</sup>Sajous, *Endocrinology*, Vol. VI, No. 2, March, 1922.

Sergent has pointed out that both physiologists and clinicians agree that the suprarenals are indispensable to life, a conclusion reached by the methods of both fields of science, and that slowly developing disease of the glands is accompanied by well marked symptoms.

"Alongside the syndrome of acute suprarenal insufficiency provoked by sudden and complete destruction of the suprarenal glands clinical observation therefore ranges syndromes of gradual insufficiency and ascribes them to progressive alteration of those glands, an alteration insufficient to suppress function totally, but quite pronounced enough to diminish it. Asthenia and hypotension are its cardinal signs. These two classes of syndromes constitute the principal clinical modalities of simple suprarenal insufficiency. When melanoderma is added, Addison's disease comes into being — a morbid complex formed apparently by a union of the symptoms of suprarenal insufficiency and those of pericapsular sympathetic irritation."<sup>1</sup>

It seems that the only uncertainty in connection with this syndrome, therefore, is in explaining the nature of the effects of the entire suprarenal gland, a problem which is as yet hardly touched.

## HYPOTHYROIDISM

Hypothyroidism is of common occurrence in general practice and as in moderately developed cases it presents a picture of general debility, rather than distinct and typical disease of the thyroid, it may conveniently be considered in connection with the other common cause of debility, hypoadrenia. It is of value, however, to first consider those cases of hypothyroidism which are typically and definitely recognizable as thyroid in character, cretinism and myxedema, as an adequate conception of these conditions, in which the numerous symptoms characteristic of thyroid hypofunction are well marked, facilitates recognition and understanding of the minor degrees of the condition in which only a few of the usual symptoms may be present.

Hypothyroidism in the young, when well marked, is termed cretinism and presents a clinical picture which is unmistakable and differs from minor degrees of hypothyroidism in forming a definite, well marked clinical type. Some authors distinguish various conditions, such as "juvenile myxedema," and limit cretinism to a congenital condition. Thus McCarrison<sup>2</sup> states:

"Cretinism is always congenital, whether endemic or sporadic. Cases of thyroid deficiency arising in the individual and due to nutritional or infectious causes should be clearly distinguished and designated as juvenile myxedema."

Cretinism, however, is generally used to designate hypothyroidism in the young and myxedema is applied to the same condition in the adult. As these are the usual connotations of these terms and as they appear to be thus firmly fixed in the literature, it seems wise to retain them.

<sup>1</sup>Sergent, *La Presse Médicale*, Oct. 12, 1921.

<sup>2</sup>"The Thyroid Gland," 1917.



Complete absence of the thyroid is rare (twelve cases were reported by Pineles). Cretinism may occur in two characteristically different types — sporadic and endemic.

**Sporadic Cretinism** Sporadic cretinism occurs in all parts of the world. Hereditary factors appear to play an important part and hereditary defective development of the thyroid apparatus has been suggested as explaining many cases of hypothyroidism, just as congenital underdevelopment of the adrenals has been described in hypoadrenia. Many such cases do not develop the characteristic symptoms of cretinism and, in fact, may exhibit few or no symptoms. They develop into the characteristic hypothyroid cases under added demands of various kinds upon their functional capacity. Cretinic symptoms may be apparent in earliest infancy or may develop during childhood. The female sex appears to be more often affected and, following the profound physiologic changes in the female organism at puberty and pregnancy, there appears to be a greater proportion affected.

In well marked cretinism and myxedema actual structural change in the thyroid is constant, varying from total absence of the gland (thyroaplasia, athyrosis) to varying degrees of degenerative change. The symptomatology is in general in direct relation to the extent of the tissue change, the fully developed cretin approaching a condition of thyroaplasia and the milder cases of hypofunction showing but small thyroid structural change. The gland may be enlarged, simple non-toxic hyperplastic goiter arising as a result of an effort to compensate for faulty functional activity, or the gland may be markedly reduced in size as a result of general atrophy. The growth is affected, particularly the skeletal system, resulting in the dwarfed condition so characteristic of cretinism. The low mentality is equally prominent. The cretin in marked cases has the mentality of an idiot and in less advanced degrees is stupid, "backward," and obviously below the normal. Facial expression is vacant and stupid. They do not behave normally at play. The skin is severely affected and may be thickened and wrinkled, and is usually dry. Mucous membranes and subcutaneous tissue show the myxedematous swelling. The fontanelles are late in closing or remain open. The skull varies from the normal and appears larger proportionately than the rest of the body. Characteristic depression of the root of the nose is said to be due to faulty development of the vomer (saddle nose). Anomalies of dentition are usual and the deciduous teeth develop slowly and may be retained. The myxedematous infiltration of the skin and mucosa gives a swollen appearance to the lips and mouth. The mucosa of the nasopharyngeal cavity is hypertrophied, the tonsils are frequently enlarged, and adenoids are common. The sexual organs are frequently underdeveloped. Deafness and partial deafness are common, though an explanation of this condition is wanting. The cheek bones are prominent, metabolism is depressed, and temperature is low. Constipation is usual. The face is sallow, pasty and colorless; the tongue protrudes from the mouth and is thickened and furrowed; the nose flattened and saddle shaped. Enuresis, possibly due to infiltration of the tissue of the neck of the bladder, is a frequent symptom. The abdomen is characteristically protuberant.

## Endemic Cretinism

When cretinism occurs as an endemic disease the condition varies considerably from the sporadic variety and it has been held that endemic cretinism or cretinic degeneration is not thyroidal in origin but is a general degenerative process involving the thyroid with the other organs of the body. Whereas sporadic cretinism is a clinical picture of advanced hypothyroidism, the endemic variety presents some symptoms and signs not explicable in such terms. Falta<sup>1</sup> states:

"There is as yet no agreement as to the question whether the manifold manifestations of the cretinic degeneration are called in to existence only by the mediation of the strumous degeneration of the thyroid gland, or a part of these are directly produced by the strumous noxus and thus are co-ordinate with the struma."

The general symptomatology of the endemic form shows much greater variety and less adherence to type than the sporadic, and in some localities individuals affected show the most marked variations in type. Endemic cretinism is well known in some localities of the world and an appreciable number of the population are affected by it. Practically all the symptoms of the sporadic variety may occur. Nervous involvement is more common and deaf-mutism is usual. "Eighty per cent. of all cretins are deaf mutes in greater or lesser degree."<sup>2</sup> The cardiac involvement, which also occurs in the sporadic form, is also common. Goiter is present in a much higher percentage of cases. Many explanations of the cause of cretinic degeneration have appeared: hereditary, chemical through the water supply, geological, bacterial. McCarrison has presented much evidence in favor of the bacterial theory. His experiments and observations over a long period of time included animal experimentation and clinical experience. He says<sup>2</sup>:

"No better illustration of the action of the toxic product of bacteria could be afforded than that which occurs in experimentally produced congenital goiter, congenital parathyroid disease and cretinism, as a result of administering cultures of fecal organisms to pregnant animals. In this observation the cultures were not killed, but there can be little question that the effects on the fetal organ were due to toxins and not to the direct action of the organisms themselves."

And again:

"This accumulation of facts demonstrates, I believe, that the causal agents of goiter, as well as of its congenital manifestations, are micro-organisms inhabiting the alimentary tract of sufferers from this disease, and often of other persons whose thyroids show no actual enlargement, but which nevertheless may be in a hyperplastic state. Except in so far that all the epidemiological and experimental facts point to anaërobic organisms as the causal agents of this disease, they do not permit of a more definite conclusion as to the identity of these organisms."

<sup>1</sup>"The Ductless Glandular Diseases," 1915.

<sup>2</sup>McCarrison, "The Thyroid Gland," 1917.

## Treatment of Endemic Cretinism

Application of the rules of general hygiene and careful inspection and maintenance of a pure water supply. Administration of iodine or iodine salts (.2 to .4 grams sodium iodide daily). Thyroid extract is particularly advisable in those cases attended with goiter. McCarrison has successfully used intestinal antiseptics, iodine, betanaphthol, thymol and salol, a form of treatment also successfully carried out by others. As the ductless glands other than the thyroid may be involved (some writers reporting pituitary involvement in as high as 95 out of 112 cases) a combination of gland substances may be tried.

McCarrison describes a type of cretinism which he terms "nervous cretinism," in which symptoms referable to the nervous system are predominant. "It may be best described as a condition of cretinous idiocy with associated cerebral diplegia and tetany, due to congenital fibrosis of the thyroid and of the parathyroid glands." This type presents many symptoms in common with the usual type, as protuberant abdomen, dwarfism, etc., but there are added the symptoms referable to the nervous system: convulsive seizures, paralysis, tetany, etc. This type seems common in India but is practically unknown in Europe and America.

**Myxedema** When previously normal individuals of adult age develop marked hypothyroidism, the condition is called myxedema. The onset is gradual, with symptoms of general asthenia, mental instability, disinclination for mental or physical work. When the condition arises suddenly, as a result of operative removal of the thyroid, the condition is sometimes called "cachexia strumipriva," a name given by Kocher. Thyroid insufficiency is attended by profound and constant effects upon general metabolism and the symptomatology is fairly constant. Falta<sup>1</sup> describes myxedema as follows:

"This condition, resulting from the absence or insufficiency of the function of the thyroid gland in the adult organism, is characterized by diminution of all vital processes and by certain trophic manifestations. The diminution affects the vegetative functions as well as the psychic life. There is found slowing of the entire metabolism and diminution of the excitability of the whole vegetative nervous system. The trophic disturbances affect especially the ectodermal tissue, the skin, hair, nails and teeth, although almost all organs may show regressive metamorphosis, especially the vascular system, which tends to be the seat of a premature arteriosclerosis."

Léopold-Lévi<sup>2</sup> stresses the pluriglandular nature of myxedema and states that while thyroid insufficiency is the predominating factor it is not the only one, and of itself will not account for the complete syndrome.

"Among the endocrine organs alone, roles of varying importance are played by the hypophysis, the thymus, the tes-

<sup>1</sup>"The Ductless Glandular Diseases," 1915.

<sup>2</sup>"Thyroid Insufficiency," Léopold-Lévi, *The Practitioner*, February, 1915.



ticles and ovaries, as well as by the pancreas, liver, etc. Derangement of these organs reacts upon the tone of the nervous system and the great sympathetic, as well as upon the constitution of the blood plasma. A portion of the symptomatology depends upon disturbance of these various glands. Briefly put, true myxedema is a pluriglandular syndrome, the predominating feature of which is thyroid insufficiency."

**Symptoms of Myxedema** The dwarfism characteristic of cretinism does not, of course, exist if the condition has developed after the normal growth process has been completed. The mental symptoms, however, are almost constantly present and may be pronounced in character. There is a characteristic apathy, dullness and disinclination for work. Normal interests are lost and there is a general slowing of thought processes. In many cases more marked symptoms, such as hallucinations and illusions may appear. The weight usually increases. The skin and mucous membranes are severely affected and surface temperature is low, as a result of the lowered metabolism. The lips, nose and cheeks have a puffed, distorted appearance. The infiltrated areas occur all over the body, although especial sites of predilection have been described — cheeks, lids, extensor surfaces, ankles, feet, supraclavicular fossae. The infiltration occurs in the mucous membranes as well as the skin and may extend to the viscera. The skin appears grayish or waxy white, and is infiltrated and furrowed. The hair is dry and brittle, with a tendency to fall out. In the case of the eyebrows, there is a tendency towards thinning of the outer third (Hertoghe's sign). The nails are dry and tend to split easily; the fingers are clubbed and spade shaped. The gums are swollen. The mucosa of the throat and glottis may be affected sufficiently to cause marked changes in the voice. The cardiac muscle is frequently affected, with resulting slowed circulation, and periods of cardiac pain. The vascular endothelium is affected and arteriosclerosis is usual (see Falta, above).

## MINOR HYPOTHYROIDISM

It has been generally recognized by all and specifically mentioned by many of the investigators in thyroid disease that the grave, well marked types (cretinism, myxedema) of hypothyroidism form a very small percentage of the total number of cases found in any locality. The great majority are those cases in which the hypothyroidism is one of lesser degree and in which many of the grosser signs and symptoms — dwarfism, idiocy, etc. — are not in evidence.

"Besides the grave form of thyroid insufficiency, of which myxedema is a maximum expression, there is a lesser thyroid insufficiency. It is of considerable importance inasmuch as, in contradistinction to myxedema, it is very frequent."

Janney<sup>2</sup> states that in its latent form hypothyroidism is of far

<sup>1</sup>Léopold-Lévi and de Rothschild, "La Petite Insuffisance Thyroïdienne et son Traitement."

<sup>2</sup>"The Diagnosis of Hypothyroidism," Janney, *California State Medical Journal*, August, 1921.

more frequent occurrence than is generally believed. In a series of cases investigated by him, he found that two-thirds showed definite hypothyroidism, although only three had been diagnosed. Janney notes, as have others, that the greatest diversity of symptoms are encountered in hypothyroidism, which are seemingly unrelated and are not explicable except by means of endocrine pathology. The action of the thyroid in affecting the metabolism of all types of cells explains the diversity of symptoms arising as a result of its diminution or withdrawal. Léopold-Lévi accounts in part for the diversity of symptoms as a result of the mediation of the sympathetic nervous system.

"In view of the influence of the thyroid gland upon the nervous system, especially the vegetative system, and upon the humoral conditions, it is readily conceivable that insufficiency of the glandular function is attended by an extremely diverse symptomatology, the expression of which is determined, in the first instance, by local predisposition, whether inherited or acquired. The syndrome includes disturbances in varying degree of all the organs the function of which is subordinated to the sympathetic system; which is in its turn dependent upon the activity of the thyroid gland."

An ever larger influence in the causation of a diversity of symptoms is given to an inherent predisposition in some tissues to react to the thyroid insufficiency.

"It sometimes happens that accentuation of a local predisposition leads to the development of an extra-thyroidic syndrome, a morbid complex which, in some cases may fitly be termed a malady, of which thyroid insufficiency is the underlying cause. For example: thyroid insufficiency is accompanied by muscular fatigue, partial neurasthenia, an ichthyotic condition of the skin, and alopecia. Now the degree of neurasthenia, myasthenia, ichthyosis, diffuse alopecia, may far exceed that which characterizes the symptoms of thyroid insufficiency, yet these signs may be due to thyroid insufficiency and in that case will respond to thyroid treatment."

### **Signs and Symptoms of Hypothyroidism**

Most of the symptoms described under cretinism and myxedema may occur in minor degree, but seldom are all, and frequently not even a considerable number, present in the same case. If the condition has existed since childhood, the individual will probably be small, poorly developed physically and of low vitality. The signs and symptoms of hypothyroidism in children particularly common are: constipation, partially closed fontanelles, mental dullness and lack of normal incentive and application in play, delayed dentition and retained and irregular teeth, deficient muscular development and disinclination for physical effort, enlarged tonsils, adenoids, impairment of hearing, pasty infiltrated skin, puffy cheeks, thick lips, scanty, dry, brittle hair, thinning of the hair on the outer third of the eyebrows, enuresis. The mentality shows all grades of defect from the idiocy of the cretin to stupidity or "backwardness." These conditions may be

evident in school work or be strikingly shown by various mentality tests. General nervousness and irritability is a common symptom. Due to deficient muscular movements of the bowel, constipation is very common in hypothyroidism, although there is also associated deficient excretion of the digestive ferments, gastric and intestinal juice, and bile, which contributes to this condition. There is a tendency to large accumulations in the colon and the intoxication resulting may give rise to symptoms which are the most prominent in the clinical picture. The condition results in a vicious circuit, for the toxemia resulting adds additional work upon the thyroid and depresses it, so that it becomes less and less efficient in correcting the intestinal condition.

In adults the symptomatology is one of general debility and lowered vitality. There is general asthenia, disinclination for physical work and inability for concentration or mental activity. Listlessness and lack of interest are characteristic. The mental symptoms are fairly constant and in advanced cases may result in definite psychoses. The temperature is subnormal and basal metabolism depressed. In marked cases this decrease is constant. Magnus Levy was the first to demonstrate this fact (1895), reporting a reduction of 58 per cent. in myxedema. This is readily conceivable when we remember the great importance of the thyroid effect in stimulating metabolism, and determination of the basal rate by the convenient apparatus now available has become an important aid in diagnosing borderline cases. The assimilation limits for glucose are raised as a result of the deficient thyroid hormone, which is essential to a normal carbohydrate metabolism. As a result of the lowered metabolism and temperature there arise the subjective symptoms of chilliness, cold extremities, etc. Joint symptoms resembling chronic rheumatism have been described (Kocher). Léopold-Lévi and de Rothschild have used thyroid therapy in such cases with constant success, although Falta cautions that this does not necessarily point to a thyrogenic origin of these conditions but may be the result of the beneficial effects of thyroid medication on general metabolism. The muscles are, however, definitely affected and become fatty, and fatigue products accumulate, giving rise to asthenia and muscular weakness. In males, impotence, and in females amenorrhea, menorrhagia and sterility are common.

The involvement of other glands described as occurring as a part of myxedema may also be present in the various grades of milder insufficiency.

"Other symptoms are frequently associated with those of thyroid insufficiency and certain among these depend for their manifestations upon the derangement of other ductless glands. The important are these:

"1. The symptoms in question are not necessarily associated with thyroid insufficiency.

"2. They may form part of the clinical complex, not of subthyroidism but of hyperthyroidism.

"3. They are associated with lesions or derangements of other endocrinic glands, and these lesions or derangements are capable, on their side, of primary or



secondary reaction upon the thyroid body, giving rise either to thyroid insufficiency or to secondary thyroid instability.”<sup>1</sup>

Certainly it would appear that the association of other glands, either as a result of thyroid disturbance or preceding it, is as a rule not sufficiently considered either in diagnosis or treatment. Thyroid therapy alone, or thyroid administration for purposes of diagnosis may be unavailing and lead to no conclusive results through neglect of this point. The hypophysis and gonads which are commonly associated in endocrine disease are frequently involved in a syndrome in which the major symptoms are those of hypothyroidism. Likewise the low blood pressure and asthenia, described above as characteristic of hypoadrenia, may be conspicuous in hypothyroidism and point to an associated suprarenal involvement.

## GENERAL CONSIDERATION OF THE SIGNS AND SYMPTOMS OF HYPOTHYROIDISM

**1. Infiltration** Infiltration is perhaps the most characteristic sign of hypothyroidism and in advanced cases gives rise to changes in practically all tissues. The pathology of many diverse signs in hypothyroidism, therefore, is the same—thickened lips, lids, skin, mucous membranes, etc. The condition is most marked in the skin and mucous membranes but may extend to practically all of the viscera. The peculiar substance which infiltrates these tissues is of unknown chemical constitution and described as mucoid. It infiltrates the connective tissue of the skin layers and muscle tissue of various organs. There is no pitting on pressure such as is seen in true edema. In minor hypothyroidism Léopold-Lévi describes a transitory infiltration appearing for brief periods and even for part of a day.

“A white indolent edema, which does not pit on pressure, makes its appearance in the vicinity of the eyelids, the forehead and the cheeks; occasionally there is transitory swelling of the feet, and the subject finds that his boots are temporarily too tight for him. Or the fingers may become sufficiently swollen to render the removal of the rings a matter of difficulty.”

Léopold-Lévi's description of this type serves to emphasize the fact that even in marked hypothyroidism the infiltrated material may vary from time to time and in some cases may even disappear.

**2. Mental and Nervous Symptoms** Symptoms referable to the nervous system and defective mental development are of constant occurrence. In congenital cretinism and marked hypothyroidism in the young, definite structural change in the brain and central nervous axis are present. The normal functioning thyroid is indispensable for the development of normal mentality. In the marked condition of cretinism typical “cretinic idiocy” is present. In lesser grades of subfunction, all gradations of mental retardation are encountered. While in total absence of the thyroid with idiocy, there is brain structural defect, in the less advanced

<sup>1</sup>Léopold-Lévi, *The Practitioner*, February, 1915.

cases and those developing in childhood this probably does not exist, as these children can be restored to almost normal mentality by thyroid therapy. Children are usually dull and stupid in the milder cases and lack the spontaneity and interests of the normal child. Definite psychoses may appear. Falta states (quoting from statistics of the English myxedema commission) that in one series studied there were found 18 cases with illusions, 16 with hallucinations and 16 with psychoses. Defects of hearing are usual, the explanations for this being numerous. General tendency to somnolence, apathy, melancholic temperament and "neurasthenia" is characteristic.

**3. Skin Appendages** The hair is typically dry, scanty, brittle and with a tendency to fall out and turn grey early. The thinning of the outer third of the eyebrow is regarded as particularly significant. The nails are brittle, split easily and show evidence of faulty formation.

**4. Metabolism** The metabolism is lowered in marked degree and is more characteristic of thyroid disturbance than of any other endocrine disease. As a result of the depressed chemical changes of the body the temperature is lowered and the skin feels cold. The patient feels chilly and is never warm. The reaction of chilliness found in hypothyroidism is characteristic and very common. The tolerance for sugar is raised.

**5. Vascular System** As noted by Falta, arteriosclerosis is a characteristic of subfunction of the thyroid. The heart may show the infiltration common to other tissues and may develop degenerative changes. One type of chilliness is described by Léopold-Lévi as due to vasomotor disturbance. "Chilliness is associated with vasomotor derangement of which aero-asphyxia, cyanosis and chilblains are the manifestations. The pulse is usually small and slow." Organic heart lesions are frequently found.

**6. Obesity** "The subthyroidic temperament is associated with tendency to obesity; in other words, the subject possesses a nutritive orientation which, under the influence of exogenous conditions, such as an overabundant dietary coupled with insufficient exercise, predisposes to the formation of fatty deposits." (Léopold-Lévi.)<sup>1</sup>

The tendency to a uniform deposition of fat is present in all cases and all ages of hypothyroidism, and seems to be bound up with the slowed metabolism and imperfect oxidation of the organism. Owing to the marked effect of thyroid therapy in these cases in reducing the fat, thyroid extract has been improperly used in the treatment of all types of obesity. Owing to its powerful action if given in sufficient dosage, fat may be burned by the organism and the weight reduced, but this is an unjustifiable and dangerous use of thyroid which should be limited to those cases which are clearly thyrogenic in origin.

**7. Constipation** Constipation is a very common symptom of hypothyroidism. Colonic stasis may become severe and the resulting intoxication a grave complication. The muscle layers

<sup>1</sup>Léopold-Lévi, *The Practitioner*, February, 1915.

of the intestine exert an imperfect, inefficient action, probably due to the lack of normal thyroid sensitization of the vegetative nervous system. In children constipation should always suggest a subfunctioning thyroid.

### 8. Asthenia and Fatigue

Fatigue, disinclination for mental and physical work, particularly in the morning, is characteristic. The infiltration of the muscle tissue, the slow oxidation and the imperfect detoxication of the body create a condition unfavorable for either mental or physical activity.

## TREATMENT

The clinical picture of hypoadrenia is that usually described as "general debility." It has been shown how intimately it is related to the infections, acute and chronic, to the lowered vitality following prolonged nervous and emotional strain, to convalescence, and to those individuals of constitutionally lowered vitality. Asthenia, low blood pressure and sub-oxidation are the conspicuous symptoms. The treatment, following the known facts of the interrelationship of the endocrine glands (considered elsewhere) and the constant involvement of the associated glands, makes a pluriglandular combination of particular value in these conditions. The particularly well established pituitary-thyroid-adrenal-gonad relationship, the effects of thyroid administration in the stimulation of the adrenals, and the relationship between the gonads and the adrenal cortex make Hormotone a rational and effective treatment for these conditions. Hormotone, as a combination of thyroid, pituitary and gonad substance, stimulates the functional activity of these glands and the adrenals (thyroid administration alone causes adrenal hypertrophy in experimental work). The effect of the suprarenals in maintaining the tonicity of the tissues innervated by the sympathetic doubtless contributes considerably to the efficiency of this formula through its stimulatory action on suprarenal function, as lessened irritability of the sympathetic appears to be characteristic of states of failing suprarenal function. Thyroid itself stimulates, sensitizes or in some manner creates a condition of greater reactivity of the sympathetic nervous system to epinephrin.

In asthenic conditions arising as a result of functional disturbance of the thyroid and pituitary, as well as the adrenals—that is, in conditions in which these are the glands predominantly at fault—it is sometimes advisable to supplement Hormotone with additional dosage of the substance of the gland to which the major symptoms appear to be referable: thus, in well marked hypoadrenia whole suprarenal substance and in hypothyroidism thyroid substance. The following case of hypoadrenia reported by Tom Williams<sup>1</sup> and treated with adrenal substance supplemented by small doses of thyroid, pituitary and gonads, is typical of the successful results of this form of pluriglandular therapy. Hormotone, a combination of thyroid, pituitary and gonads, when supplemented by adrenal substance in such cases of hypoadrenia, has proved its value through years of clinical trial by the ablest in the profession.

"*Vagotonic Hypoadrenia.* A young lawyer was referred last winter by Dr. Wilmer, to whom he had been sent because of

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<sup>1</sup>Tom Williams, *Medical Record*, April 14, 1917.



distress during prolonged use of the eyes. There were no physical abnormalities sufficient to account for this, so Dr. Wilmer referred the patient to me for neurological survey, partly because of an apprehensiveness which the patient had developed as a boy and because of an increasing lack of stamina, indigestion and paresthesiae. Examination showed a low blood pressure, 110 and 72, decreasing on standing, the following day falling to 90 and 62, increasing to 102 on standing. Pulse 102; positive Ascher phenomenon, positive Trousseau sign, Chvostek sign however absent, and history of tetanic cramp and paresthesiae in the legs after prolonged sitting. The reaction to pilocarpine was excessive, there being chills, nausea, weakness, and urethral dragging pain. Treatment of the hypoadrenia alone by adrenal substance caused considerable improvement. This was later augmented by small doses of thyroid, pituitary, and gonads, when great improvement followed."

In asthenia with marked suboxidation and lowered metabolism and evidence of general hypothyroidism, the addition of thyroid may be exceedingly valuable. The general results of thyroid therapy are among the most striking observed in medicine and in definitely diagnosed, uncomplicated hypothyroidism the administration of thyroid extract alone may be sufficient. In cretinism and myxedema the improvement in the mentality and physical symptomatology may result in a return to a close approximation to normal. This improvement is usually prompt, a few days sufficing to bring an easily discernible change. The dosage is from 1 to as much as 5 grains daily, the greater number of cases requiring low dosage — from 1 to 2 grains daily. In minor hypothyroidism the effects are most gratifying and low dosage is advisable.

It will be noted that in "general debility" with asthenia, suboxidation, low blood pressure, mental and physical lassitude, lack of "drive," etc., as the cardinal symptoms, there is usually defect of cell metabolism itself. In hypoadrenia and in hypothyroidism there is accumulation of the catabolic products, fatigue substances, and (in hypothyroidism) definite infiltration of the tissues of the body. The effect of Hormotone is one of stimulation of the entire group of glands described by Falta as the acceleratory or dissimilatory, and is attended by stimulation of the lowered metabolic processes, increase in respiratory quotient, stimulation of the tissues innervated by the sympathetic, correction of suboxidation and the resulting accumulation of fatigue substances, and increase in adrenal function, which has been shown to be so essential in the maintenance of muscle efficiency and the prevention of fatigue and asthenia.

The frequent association of functional disturbances of the thyroid, hypophysis, suprarenals and gonads, with the resulting clinical picture that is not characteristic of pure type disturbance of any single gland, has been described. These complex involvements account for the great majority of the cases of general debility and "run-down" conditions, which certainly form one of the most numerous groups met with in general practice. In the treatment of these cases it is unnecessary to relate the in-

sufficiency of the usual "tonic" drugs or to note the fact that the endocrine substances used in medicine are the only ones which definitely raise lowered basal metabolism. The advisability and even necessity of combined therapy has been shown.

"Where thyroid insufficiency is associated with other endocrine insufficiencies, the glandular therapy should be equally complex; ovarian, testicular, suprarenal and pituitary extracts may all be employed with advantage in suitable cases." (Léopold-Lévi.)

### **Summary of Treatment**

In simple asthenia, without disproportionate involvement of any particular gland, Hormotone, in a dosage of 1 or 2 tablets three times daily.

In cases of determinable involvement of the suprarenals — hypoadrenia — in which the adrenal factor is predominant, Hormotone in a dosage of 1 or 2 tablets three times daily, supplemented with 1 tablet (2 or 5 gr.) of Entire Suprarenal Substance.

In cases with involvement of the thyroid, 1 or 2 Hormotone Tablets three times daily, supplemented with 1 tablet (1/10 to 1½ grs.) of Thyroid Substance, the thyroid dosage depending upon the extent of the symptoms of hypothyroidism.

## **SENILITY**

The similarity in general appearance of cases of well marked hypothyroidism and senility has frequently been noted, in both the psychic and physical features of the two conditions. The characteristic mentality of the aged, with its loss of memory, tendency to somnolence and lack of grasp of difficult or complex matter, has its counterpart in the mentality of marked hypothyroidism. The impaired hearing, dry and scanty hair, lowered or lost sex function, and arteriosclerosis, of the one are likewise characteristic of the other. Horsley, in particular, and others following him, noted the increase in connective tissue and the alteration in the skin as common to both conditions.

### **Senile Changes Pluriglandular In Origin**

In senility, however, and particularly in premature senility, considerations of clinical observation, as well as the physiological correlation of the endocrine glands, warrant the belief that premature senility is not due to subfunction of the thyroid alone, diverse and widespread as these effects are.

"For reasons less obvious and in a manner less dramatic than the menopause, the conditions surrounding the mere advance of years tend to produce inadequacy of the thyroid function. It is not that the thyroid gland declines more rapidly than the other internal secretory glands, for all of them, even including the spleen, tend to diminish both in size and activity as the years advance. It is that the thyroid gland is so important to the economy that any diminution in its activities reflects itself unmistakably in a great many directions."<sup>1</sup>

<sup>1</sup>Leonard Williams, "Minor Maladies," 1918.

Certain symptoms and signs indicate the involvement of other endocrine tissues and the condition of senility very probably arises as a result of a gradual pluriglandular hypofunction. "Besides the thyroid there are also different other ductless glands whose degeneration produces old age. These are the sexual glands, the pituitary body and the adrenals."<sup>1</sup> Falta is in accord with this opinion in so far as it is applied to premature senility. He says:

"In a detailed study Lorand has upheld the idea that the degeneration of the ductless glandular system is chiefly the cause of senility. I would not concur with this, so far as physiological old age is concerned, but believe much more, as does also Ewald, that the ductless glandular system like every other organ participates in the involution of old age. There is on the other hand a pathological old age, setting in prematurely or associated with distinct accentuation of the cachexia. The premature senility which develops in most of the diseases due to giving out of function, and especially in multiple ductless glandular sclerosis, makes intelligible to me the fact that degeneration in the ductless glandular system may be one of the causes of pathological age."<sup>2</sup>

### Autointoxication

The conception of autointoxication as a contributing factor in old age has also been brought into relation with pluriglandular endocrine involvement by many authors and such intoxication seems to follow as a necessary part of the glandular disturbance. Both the adrenals and thyroid, which play an important part in the antitoxic mechanism of the body, fail to exert their normal antitoxic action and the widespread systemic effects of the intestinal toxins proceed unhindered.

"In true senescence, normal decline, the outstanding phenomena have to do with degeneration of the ductless glands. Since these glands regulate the effects of self poisoning, when they fail of their integrity, autointoxication progresses almost unhindered."<sup>3</sup>

The effects of adrenal insufficiency in establishing a premature senility have been noted and these effects may be found in the diverse symptomatology of senility. Sajous assigns an important place to the adrenals in this condition.

"In the light of the data I have submitted, however, it is clear that the lesions to which the adrenals are subjected during infection and autointoxication, from birth to the last day of life, do greatly shorten it by limiting the functional area of the organs through the fibrosis they entail. It is quite probable, in fact, that centenarians owe their prolonged longevity mainly to integrity of their adrenals."<sup>4</sup>

<sup>1</sup>Lorand, "Life Shortening Habits and Rejuvenation," 1922.

<sup>2</sup>Falta, "The Ductless Glandular Diseases," 1915.

<sup>3</sup>J. Madison Taylor, *Medical Record*, Nov. 3, 1917.

<sup>4</sup>Sajous, "The Internal Secretions and the Principles of Medicine," 10th Edition, 1922.



## Emotional Factors

The effects of prolonged and intense emotional and psychic activity have been stated to contribute to premature senility by many physicians and the idea is current among the laity as well. If the reservation is made that a moderate normal mental activity is necessary to the prolongation of life, the importance of excessive emotional and psychic activity in causing senile changes will probably be doubted by none. Taylor says:

"Conditions of fierce, frantic competition, breeding as they do envy, hatred and malice; inviting to indiscretions in act, in amusements, in food, in drink, irregularity in hours of sleep, inadequate forms and kinds of rest and exercise, form the foundation of and supply favorable conditions for presenility. Hence it comes to pass that when these unfortunates reach early middle age they show the earmarks of overcombustion, disintegration, cellular decline."<sup>1</sup>

Having important bearing upon the mechanism of these emotional states would appear to be the work of Cannon, who demonstrated the effects of the strong emotions, fear, rage, etc., in causing a great increase in adrenal activity and epinephrin output. It seems probable that an individual whose mental life has been filled with a succession of such states develops an early functional incapacity of the adrenals and a consequent early appearance of the signs of senility.

## Influence of the Sex Glands

The influence of the sex glands in maintaining physical and mental vigor has long been known and the development of signs and symptoms of senility following castration is of constant occurrence. This relationship has within the last few years been emphasized by the experiments of Steinach, both by transplanting sex glands and by effecting a stimulus to the individual male gonad by vasectomy. In these experiments upon old and decrepit animals (male and female) the transplantation of ovaries and testes made the most remarkable change in the animal. Animals previously feeble, decrepit and unfit for breeding purposes gained in physical vigor and appearance, and became sexually potent. In commenting upon these experiments Lorand says:

"It is interesting to note that at the autopsy of these rejuvenated old rats the sexual organs, including the ovaries, mammary glands, and uterus, were found in the same condition as would have been expected in young rats.

"Thus, upon transplantation of the ovaries of young rats into old ones, the new ovaries made up for the lost functions of the former ovaries which had undergone degeneration by reason of advanced age. Along with this came the remarkable transformation into a young animal, with all the attributes of a young female, again proving the truth of what the great Belgian physician, Jean Batiste Helmont, said several centuries ago, *viz.*, that a woman is made what she is by her ovaries."<sup>2</sup>

<sup>1</sup>Taylor, *Medical Record*, Nov. 3, 1917.

<sup>2</sup>Lorand, "Life Shortening Habits and Rejuvenation," 1922.

The gonad influence on the organism is very marked and in young adult life affects not only the physical but the mental development as well.

"Nearly all the great men of present and past times, including great writers, artists, famous generals, etc., have had highly developed sexual proclivities. Their high grade intellect offers an enormous contrast to the inferior mental qualities and feeble intellect of castrates."<sup>1</sup>

The onset and development of the condition of premature senility seems to be intimately connected with the endocrine glands, even such factors as autointoxication, emotional strain, etc., acting through them. Various observers have placed emphasis upon this or that gland, all, however, recognizing the pluriglandular nature of the process. The thyroid and gonads appear to be central figures in the causation, although it is by no means believed that they are the only ones. The thyroid element has been discussed and is of such a nature that premature senility has been likened to hypothyroidism. The influence of the thyroid upon all tissues of the body makes its importance in this connection easily understood. The influence of the gonads is scarcely less striking, and the experimental work has served to emphasize the function of this tissue in maintaining and restoring the vital processes characteristic of youth. The part of the adrenals, while not so strikingly apparent as the thyroid and gonads, seems to be important. Premature senility, then, is a condition the establishment of which involves a definite group of glands and is not wholly dependent upon any one of them.

## TREATMENT

The effects of organotherapy in bringing about an amelioration of the symptoms, and as a preventive measure in delaying their appearance, has been thoroughly demonstrated. The correction of vicious modes of living and habits is of prime importance and excessive indulgence in food, alcohol, tobacco, work and stimulants of any kind should be avoided in any treatment looking toward the rejuvenation of the individual. Organotherapy should be used in conjunction and the prognosis is most favorable.

"Old age being caused by degeneration of the endocrine glands, especially the thyroid and sexual glands, all that is necessary to secure rejuvenation is to improve the condition of these glands. The best and easiest way to do this is to administer by the mouth extracts of these glands, after their extirpation from healthy animals. As long as thirty or more years ago it was proved that when one of these glands, such as the thyroid, is degenerated, all of the normal functions of this gland can be reproduced by ingesting extracts of the thyroid of sheep. The diseased gland is thus successfully replaced by the ingestion of the animal gland.

"To bring about rejuvenation I have given to old men and women, and also to persons suffering from premature old age, extracts of the thyroid and sexual glands of animals. As al-

ready mentioned, marked success attended the procedure. The persons treated looked considerably younger after it, to the extent of ten or fifteen years and sometimes even more. The wrinkles in the face already began to disappear four or five weeks after the treatment, and at the same time, previously corpulent persons, losing their excess of fat, were made to look slender, thus imparting a youthful impression."<sup>1</sup>

In a discussion of the neurotic and neurasthenic conditions arising in elderly women Leonard Williams says:

"Of polyglandular therapy I have not had very much experience but since I have been using a mitrailleuse called Hormotone I have had considerable success in those cases just referred to as benefited by pituitary."<sup>2</sup>

Hormotone in a dosage of 1 or 2 tablets t. i. d. is usually sufficient and the effects in restoring physical and mental vigor are most encouraging. The added strength and sense of well-being and the maintenance of the physical and mental vigor are not only satisfying to the individual himself but are of interest and value to society as well, for at a time when the maximum of intellectual efficiency, through education and years of experience, has been reached, the retrograde changes of senility ordinarily remove in large measure the productive and creative capacity and the value of the individual is lost to society. Any system of treatment, therefore, which will add, by rejuvenation effects, any considerable period of vigor and usefulness to the period of life in which the highest attainment is possible, is of more than ordinary interest to the physician and to society.

## CLINICAL REPORTS

———, Miss.

"I have a case of hypothyroidism that I have had taking your Hormotone for two weeks (2 tablets three times a day before meals) with the most satisfactory results so far. Pulse reduced from 120 to 108 per minute, nervous symptoms much improved, and has gained 9 pounds in weight (in two weeks). It is too early of course, to be sure, but it looks like she is going to get well, and is taking nothing but Hormotone.'

———, N. Y.

"Some time ago your representative left with me a sample of Hormotone, and you later sent me a bottle of same. Shortly after this I had a case of chronic gastrointestinal toxemia with very weak heart action and blood pressure systolic 120, diastolic 100. The case was a man 50 years of age. He was put on Hormotone, the sample of same coming in very handy. He was given nothing else but this and castor oil, and animal food was withheld from diet. There was marked improvement in this case in a couple of days and continued improvement. He

<sup>1</sup>Lorand, "Life Shortening Habits and Rejuvenation," 1922.

<sup>2</sup>"Discussion on the Therapeutic Value of Hormones", at a meeting of the Therapeutic and Pharmacological Section of the Royal Society of Medicine, London, January 20, 1914.



was perfectly well in a week, and it was surprising to me to see the quick improvement in heart action and rise in the blood pressure. I am taking increasing interest in organotherapy, and desire literature and list of your products."

———, N. J.

"I have given a two weeks' treatment of your Hormotone to a cretin, age 18 months, and the mother is delighted with the improvement. I wish to continue treatment. I enclose check for \$1.00. I have no price list. Please send me a dollar's worth by parcel post, and oblige."

———, MAINE.

"I have a patient, a lady, who had been operated upon for thyroidectomy and was continually losing flesh, impaired digestion, nervous and unable to do her household duties, but some relief from thyroid gland tablets. I advised Hormotone, and the treatment still continues, with complete recovery and a gain of some 15 pounds in weight."

DETROIT, MICH.

"In neurasthenic conditions I have obtained unvarying success through the administration of Hormotone. I obtained remarkable results recently in administering in tablet form three times daily to an octogenarian on the verge of complete senile debility. I unhesitatingly employ it wherever I deem it is indicated."

———, ARKANSAS.

"Inclosed you will find \$4.90 for which please send me 500 Hormotone Tablets. I have used all I could get from our retail druggist. They are the finest medicine for old people that are suffering from indigestion and senility that I have ever found. Please send them as soon as you can."

———, MAINE.

"I am pleased to say I secured some very satisfactory results with the two bottles of Hormotone you sent me some time ago. I tried them in a neurasthenic of advanced years and he reported that he felt at least ten years younger after taking the last bottle."

———, VERMONT.

"My patient has received the most excellent results from the Hormotone Tablets you so kindly forwarded. He was suffering from a low asthenic condition, blood pressure only 120, as a result of a severe attack of stomach gripe two years ago. Blood pressure is now 132, general condition much better. No fainting spells in past six weeks. Attacks previously occurred every ten or twelve days, rendering him almost helpless for a few days following. Enclosed find one dollar for another bottle."

# HORMOTONE

in

## PREMATURE SENILITY

and

## OLD AGE

**Stimulates metabolism**

**Increases muscle  
tonicity**

**Raises respiratory  
exchange**

**Effects marked sub-  
jective improvement**

---

*Dose:* 1 or 2 tablets  
three times daily



**G. W. CARNRICK CO.**

**417-421 Canal Street**

**New York, N. Y.**

# SPECIAL FORMULAE

Each formula is sold in bottles of 40 and 100 capsules or tablets.

## No. 1 Pluriglandular Comp. Male

Hypoadrenia, Asthenia, Low Blood Pressure, Fatigue Syndrome

Thyroid grs. 1/10  
 Pituitary " 1/40  
 Suprarenal " 1/4  
 Orchic " 1/4  
 Physiological Salts Comp. " 1/4

Dose: 1 or 2 capsules 3 times daily.

## No. 2 Pluriglandular Comp. Female

Hypoadrenia, Asthenia, Low Blood Pressure, Fatigue Syndrome

Thyroid grs. 1/10  
 Pituitary " 1/40  
 Suprarenal " 1/4  
 Ovarian " 1/4  
 Physiological Salts Comp. " 1/4

Dose: 1 or 2 capsules 3 times daily.

## No. 3 Pineal Comp. Male

Backward Children, Mongolism, Retarded Mental or Physical Development

Anterior Pituitary grs. 1/5  
 Thyroid " 1/2  
 Suprarenal " 1  
 Orchic " 1 1/2  
 Pineal " 1/30  
 Physiological Salts Comp. " 1/4

Dose: 1 or 2 capsules 3 times daily.

## No. 4 Pineal Comp. Female

Backward Children, Mongolism, Retarded Mental or Physical Development

Anterior Pituitary grs. 1/5  
 Thyroid " 1/2  
 Suprarenal " 1  
 Ovarian " 1 1/2  
 Pineal " 1/30  
 Physiological Salts Comp. " 1/4

Dose: 1 or 2 capsules 3 times daily.

## No. 5 Orchic-Prostate Comp.

Enlarged Prostate, Sexual Neurasthenia, Vesical Irritation

Orchic grs. 1  
 Prostate " 2  
 Calcium Glycerophosphate " 2

Dose: 2 or 3 capsules 3 times daily.

## No. 6 Corpus Luteum Comp.

Vomiting of Pregnancy (Hyperemesis Gravidarum), Menstruation Psychosis, Mild Manic Depressive Insanity (Females)

Corpus Luteum grs. 1  
 Thyroid " 1/10  
 Physiological Salts Comp. " 1/4

Dose: 1 to 3 tablets every 3 or 4 hours, which may be increased to 5 tablets in unusually severe cases.

## No. 7 Parathyroid Comp.

Tetany, Uremia, Epilepsy, Paralysis Agitans, Nervous Tremor of Children

Parathyroid grs. 1/20  
 Orchic " 1  
 Calcium Lactate " 2

Dose: 2 or 3 capsules 3 times daily.

## No. 7 N. P. Parathyroid Comp.

Tetany, Uremia, Epilepsy, Paralysis Agitans, Nervous Tremor of Children

Parathyroid Nucleo Protein grs. 1/20  
 Orchic " 1  
 Calcium Lactate " 2

Dose: 2 or 3 capsules 3 times daily.

## No. 8 Thymus Comp.

Chronic Arthritis, Rheumatoid Arthritis, Arthritis Deformans

Thymus grs. 3  
 Thyroid " 1/10  
 Pituitary " 1/20

Dose: 1 or 2 tablets 3 times daily.

## No. 9 Mammary Comp.

Menorrhagia, Metrorrhagia, Subinvolution, Prolonged Menses, Uterine Oozing

Mammary grs. 2  
 Posterior Pituitary " 1/4  
 Calcium Lactate " 2

Dose: 1 tablet 3 times daily.

## No. 10 Suprarenal-Pituitary Comp.

Asthma, Bronchial Asthma

Suprarenal grs. 2  
 Pituitary Entire " 1  
 Thyroid " 1/10  
 Anterior Pituitary " 1 1/2  
 Physiological Salts Comp. " 1/4

Dose: 1 or 2 tablets 3 times daily, which may be increased when asthmatic aura appears.

## No. 11 Ovarian Comp.

Amenorrhea, Ovarian Hypofunction, Menopause.

Ovarian Substance grs. 3  
 Thyroid " 1/10  
 Physiological Salts Comp. " 1/4

Dose: 1 or 2 tablets 3 times daily, which may be increased to 3 or 4 tablets from 5 to 10 days before the expected menstrual period.

## No. 12 Renal-Pancreas Comp.

Nephritis, Prevention of Uremia.

Kidney Substance grs. 2  
 Pancreas Sub. " 2  
 Physiological Salts Comp. " 1/4

Dose: 1 or 2 tablets 3 times daily.



<b>TRYPSOGEN</b> <b>Tablets</b>	Diabetes mellitus; glycosuria and defective carbohydrate metabolism. Also useful in certain pancreatic disorders, and as an adjunct in hypertension. <i>May be had without gold and arsenic at same prices.</i>	100 500 1000	<b>SECRETOGEN</b> <b>Tablets</b>	A physiological treatment of gastrointestinal insufficiencies and constipation, intestinal stasis, infantile diarrheas, marasmus and inanition.	100 500 1000
<b>Capsules</b>		100		Tablets. A homostimulative extract from the duodenum.	1/2 pt.
<b>Caps. Dble. St'ngth</b>	Presents the homostimulative principles that excite the production of the internal secretion of the pancreas when the gland is functionally deficient; contains proteolytic and lipolytic ferments; also 1/200 gr. each of gold bromide and arsenic bromide.	100		Dose: 1 to 3 tablets before or after meals.	1 pt.
				Elixir. A homostimulative extract from the stomach and duodenum; contains 1/10 of 1% HCl.	5 pts.
	Dose: 1 to 3 capsules after meals.			Dose: 1 to 3 teaspoonfuls before or after meals.	1 gal.
<b>HORMOTONE</b>			<b>KINAZYME</b>	An aid to metabolism in tuberculosis and other wasting diseases; especially valuable in undernourished and backward children.	100
<b>Tablets only</b>	Neurasthenia; "run down conditions"; sub-oxidation; neuroses; menstrual and climacteric disorders; cardiac asthenia; hypotension, etc. A combination of tonic hormones from thyroid, pituitary, adrenal and gonads.	100	<b>Tablets</b>		500
	Dose: 2 to 7 tablets or 1 to 3 capsules after meals.	500	<b>Capsules</b>	Contains 1/60 gr. whole pituitary in addition to pancreas, liver and spleen substance with calcium phosphate. Kinazyme (Old Formula) contains the same without pituitary. Same price as Kinazyme.	1000
	Dose: 1 or 2 tablets 3 times daily before meals.	1000		Dose: 2 to 4 tablets or capsules after eating.	100
<b>HORMOTONE</b> <b>w/o Post-Pituitary</b>	In neurasthenia associated with hypertension.	100			
	Dose: 1 or 2 tablets 3 times daily before meals.	500	<b>FEROVARIN</b>	To increase red corpuscles and hemoglobin content of blood in anemia and chlorosis.	50
<b>VIRILIGEN</b>	Indicated in lowered virility and sexual neurasthenia of functional origin.	100	<b>Tablets</b>	Contains 1/30 gr. of desiccated thyroid combined with desiccated entire ovary and the salts of the blood plasma in physiological proportions.	100
<b>Tablets</b>				Dose: 1 or 2 tablets or capsules 3 times daily after meals.	500
<b>Capsules</b>	Presents desiccated extracts of anterior pituitary, suprarenal cortex, lymph, brain and spinal cord substance, testis and 1/10 gr. thyroid. Not sold in bulk nor sampled.	100	<b>Capsules</b>		1000
	Dose: 1 or 2 tablets or capsules 3 times daily before meals.	1/2 doz.	<b>Alkaline Tablet</b> (G.W.C.Co.)	A coated tablet containing salts of sodium potassium and calcium in physiological proportions.	200
<b>Ampoules</b>				A valuable medication in hypo-alkalinity.	500
<b>MAMMAGEN</b>	To increase lactation in deficient milk supply in the nursing mother. Each tablet contains 1/2 grain desiccated entire pituitary substance with the hormones and vitamins of corpus luteum, placenta and mammary glands.	50	<b>PERISTALSIS COMP.</b> (G.W.C.Co.)	A combination of the peristaltic principles of the duodenum, pylorus and spleen, together with 1/2 grain of purified ox gall and 1/4 grain pituitary.	40
<b>Tablets</b>		100	<b>Coated Tablets</b>	Dose: 1 to 3 tablets after supper and at bedtime.	100
<b>Capsules</b>	Dose: 1 or 2 tablets or capsules 3 times daily after meals.	500			
		1000			

# SINGLE GLAND PRODUCTS

Our organotherapeutic products are made from fresh glands of healthy food animals, in our own laboratory, under the supervision of competent chemists. All moisture has been removed from these gland products and they will keep indefinitely if contents are not exposed to moisture and bottle is kept tightly corked.

	In one bottle		In one bottle
Albuzyme	caps. 75	Ovary w/o	Powder oz.
Amylzyme	Powder oz.	Corpus Lut.	5-gr. caps. 100
	caps. 40		
	100	Ox Gall	Powder oz.
Brain	Powder oz.	Pancreas	Powder oz.
Brain & Spinal Cord	2-gr. tabs. 100		5-gr. caps. 100
Corpus Luteum	Powder 1/2 oz.	Pancreatin (U.S.P.)	Powder oz.
	oz. 50		2-gr. tabs. 100
	100		5-gr. caps. 100
	5-gr. tabs. 50	Pancreatin & Soda	Tablets 100
	100		
	5-gr. caps. 50	Parathyroid	Powder 1/2 oz.
	100		1/20-gr. tabs. 100
1 c. c. ampoules, 20% 1/2 doz.			
Duodenal Sub.	Powder oz.	Parotid	Powder oz.
Epinephrine	Powder 1 grain		
	Chloride Sol., 1-1000 oz.	Pepsin (U.S.P.)	Powder oz.
1 c. c. ampoules, 1:10,000 1/2 doz.			
Glycogen	Powder 1 gram	Pineal Gland	Powder 1/2 oz.
	1/4 oz.		1/10-gr. tabs. 100
	1/2 oz.		
	1 oz.	Pituitary	Powder 1/2 oz.
2 c. c. ampoules (box of 6)			1 oz.
Kidney	Powder oz.		1/2-gr. tabs. 50
	2-gr. tabs. 100		100
	5-gr. caps. 100		1-gr. tabs. 50
Lecithin	1/2 oz. jars		100
" Commercial	1 oz. jars		2-gr. tabs. 50
			100
Liver	Powder oz.	Pituitary, Ant.	Powder 1/2 oz.
	3-gr. tabs. 100		1 oz.
	5-gr. caps. 100		1-gr. tabs. 50
Lymphatic Gl.	Powder oz.		100
	3-gr. tabs. 100		2-gr. tabs. 50
			100
Mammary Sub.	Powder oz.		
	3-gr. tabs. 100		
	5-gr. caps. 100		
Marrow—Red	1/2 pt.	Pituitary, Post.	Powder 1/2 oz.
Bone Glycerole	1 pt.		1/10-gr. tabs. 100
			1/2-gr. tabs. 100
Orchic Sub.	Powder oz.		(Liquor Hypophysis)
	2-gr. tabs. 100		1/2 c. c. ampoules, Ob., 1/2 doz.
	5-gr. caps. 100		1 " " 1/2 doz.
Ovarian Sub.	Powder oz.		1 c. c. ampoules, Surg., 1/2 doz.
	2-gr. tabs. 100		
	5-gr. tabs. 50	Placenta	Powder oz.
	100		3-gr. tabs. 100
	5-gr. caps. 50		5-gr. caps. 50
	100		100

Prostate	In one bottle		Thyroid (U.S.P.) (cont.)	In one bottle	
	Powder	oz.		½-gr. tabs.	100
	2-gr. tabs.	100		1-gr. tabs.	100
	3-gr. caps.	100		2-gr. tabs.	100
Spleen	Powder	oz.		1-gr. caps.	100
	3-gr. tabs.	100		2-gr. caps.	100
	5-gr. caps.	100		3-gr. caps.	100
				5-gr. caps.	100
Steapzyme	caps.	75	Tonsil	Powder	oz.
				3-gr. caps.	100
Suprarenal Gland (U.S.P.)	Powder	oz.	<b>Nucleo-Protein Products</b>		
	1-gr. tabs.	100			
	3-gr. caps.	100			
Suprarenal Cortex	Powder	⅛ oz.	Ovarian	Nucleo-protein	10%
		1 oz.			100 Tablets
	1-gr. tabs.	50	Parathyroid	Nucleo-protein	5%
		100			20 Tablets
	2-gr. tabs.	50	Pituitary	Nucleo-protein	10%
	100			20 Tablets	
Suprarenal Medulla	3-gr. caps.	50	Suprarenal	Nucleo-protein	10%
					100 Tablets
	Powder	¼ oz.	Thyroid	Nucleo-protein	1%
Thymus	2-gr. tabs.	100			100 Tablets
	Powder	oz.	“	Nucleo-protein	5%
	3-gr. tabs.	100			100 Tablets
Thyroid (U.S.P.)	5-gr. caps.	100	“	Nucleo-protein	10%
	Powder	oz.			100 Tablets
	1/10-gr. tabs.	100	“	Residue	½ oz.
	¼-gr. tabs.	100			

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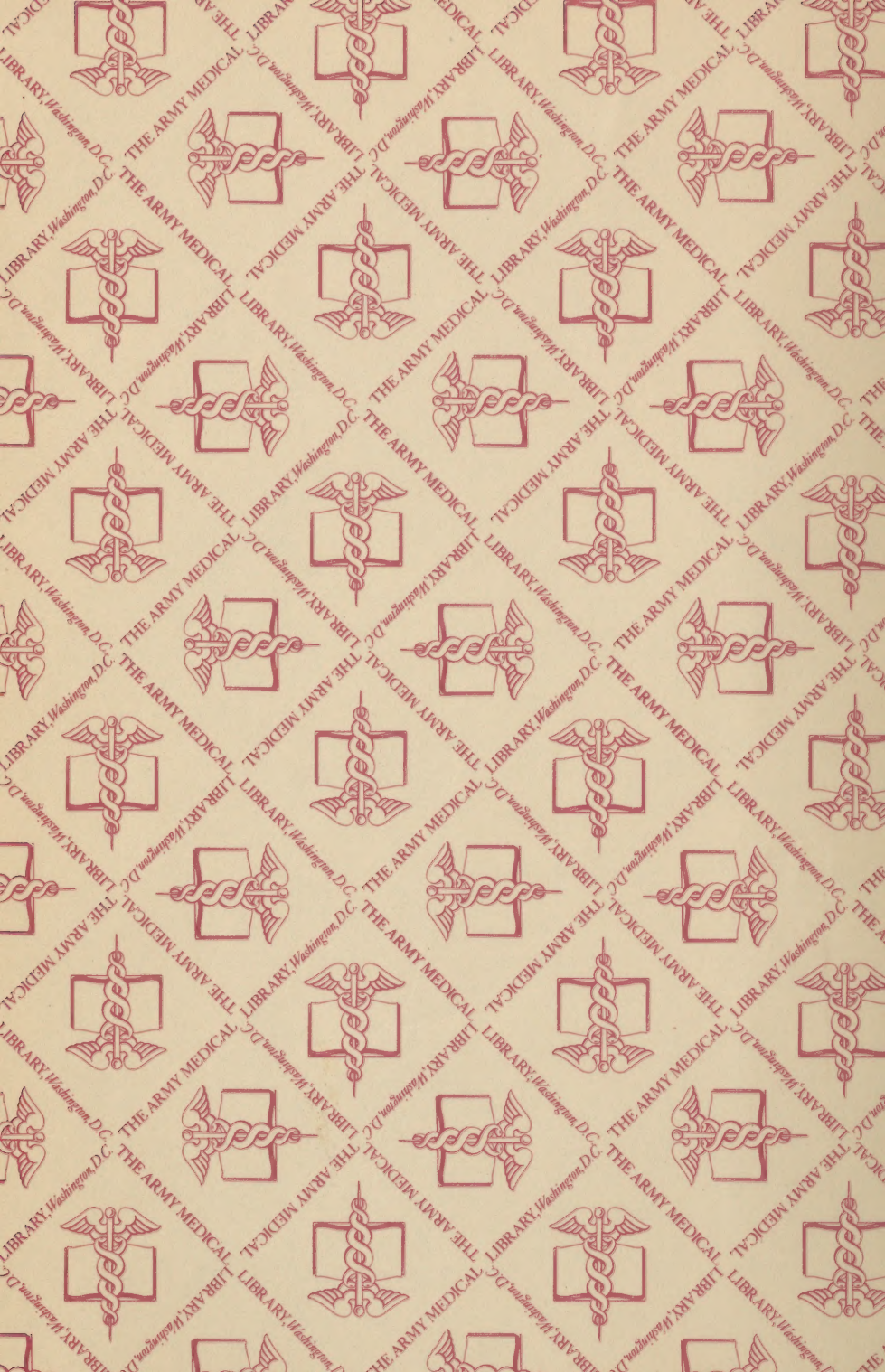












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